K003267

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Summary of Safety and Effectiveness
AUTO™ D-Dimer CRS 126-A

Sigma Diagnostics AUTO D-Dimer™ is a polystyrene microparticle agglutination assay for the quantitative determination of fibrin degradation products containing D-dimer in citrated human plasma using automated coagulation analyzers.

Activation of the hemostatic system produces stabilized or cross-linked fibrin as its end-product. The hydrolysis of fibrinogen molecules to form fibrin opens sites which allows the formation of affinity driven ternary complexes of fibrin, tissue plasminogen activator, and plasminogen, resulting in the formation of plasmin. Plasmin will cleave the cross-linked fibrin to form fibrin degradation products (FDP). Among these degradation products are species which contain factor XIII mediated transglutaminase (lysine-glutamine) linkages between the carboxy terminal regions of adjacent fibrin(ogen) gamma chains. The globular domains containing these gamma chains are often referred to as D-domains and fibrin degradation products containing adjacent d-domains crosslinked by factor XIII are called D-dimers. Antibodies have been developed which recognize epitopes for D-dimer fibrin.(1),(2)

Higher than normal levels of D-dimer in plasma would appear to indicate the activation of coagulation with the formation of crosslinked fibrin and the subsequent proteolysis to release D-dimer containing breakdown products. Elevated levels have been observed in disseminated intravascular coagulation (DIC) (1), deep venous thrombosis (DVT) (2,3,4) and pulmonary embolism (PE) (5) and in other disease states such as cancer (6). D-dimer levels may rise in a normal pregnancy, but higher levels may indicate complications (7). Therefore, the presence of elevated D-dimer levels therefore is not sufficient for the diagnosis of a thrombotic disorder. However, the absence of elevated D-dimer levels may be used to help rule out the presence of a thrombotic disorder, such as DIC, DVT or PE.

In the Sigma AUTO D-Dimer assay, the polystyrene micro particles have monoclonal antibody attached covalently. In the presence of multimeric D-dimer antigen a complex forms. The formation of the complexes causes an increase in the absorbance of the reaction mixture that is correlated to the antigen level. The Sigma procedure provides a means to quantitatively measure plasma levels of D-dimer. The D-dimer level may be used to determine patient management strategies.

The monoclonal antibody used in this kit is specific for D-dimer by virtue of the screening method used in the selection of the hybridoma.(3) A hybridoma secreting antibody which reacted positively with purified D-dimer but not with the whole fibrinogen and fragment D of fibrinogen was selected.

The safety and effectiveness of Sigma Diagnostics' AUTO D-Dimer kit has been demonstrated by showing its substantial equivalence to Stago's ASSERCHROM D-Di kit. Both kits were compared using normal and abnormal samples. Sigma's AUTO D-Dimer reagent (Y) was used on an AMAX 190 Plus and Stago's ASSERACHROM D-Di

kit (X) was run, following their insert, using an approved ELISA plate reader. Results of these correlation studies are presented in the table below.

Instrument	**AMAX 190 Plus**
Regression Equation	y = 0.5629x – 35.8
Correlation Coefficient (r)	0.937
Number of Samples	135

Precision studies demonstrated a within run CV of less than 4% and a total precision of less than 7%, using low and high abnormal control plasmas. Sigma's AUTO D-Dimer kit has an analytical sensitivity of 15 ng/mL. The reportable range for undiluted samples is 15-3200 ng/mL. If the result exceeds the reportable range, retest the sample using an appropriate dilution. No antigen excess hook effect is observed at D-dimer levels below 60,000 ng/mL.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
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MAR 1 5 2001

William R. Gilbert, Ph.D.
Manager, Scientific Affairs
Sigma Diagnostics, Inc.
545 South Ewing Avenue
St. Louis, Missouri 63103

Re: K003267
Trade Name: Sigma Diagnostics AUTO D-Dimer
Regulatory Class: II
Product Code: DAP
Dated: February 14, 2001
Received: February 20, 2001

Dear Dr. Gilbert:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known): K003267

Device Name: Sigma Diagnostics AUTO D-Dimer

Indications For Use:

Sigma Diagnostics AUTO D-Dimer is a particle-enhanced turbidimetric immunoassay used to detect and measure crosslinked fibrin degradation products containing the D-dimer in human plasma and aids in detecting the presence and degree of intravascular coagulation and fibrinolysis (the dissolution of the fibrin in a blood clot) and in monitoring therapy for disseminated intravascular coagulation (nonlocalized clotting in the blood vessels).

Joseph Z. Hackett

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K003267

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use____ OR **Over-The-Counter Use** ____
(Per 21 CFR 801.109)